

96
78. The combination of two or more antibodies of claim 75 comprising CBH-7 and CBH-4D.

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80. The combination of two or more antibodies of claim 75 comprising CBH-7 and CBH-17.

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81. A pharmaceutical composition comprising the antibodies of claim 75, 76, 77, 78, 79, or 80 and a pharmaceutically acceptable excipient.

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82. A method of treating a patient infected with HCV, the method comprising steps of:
providing a patient infected with HCV or susceptible to HCV infection; and
administering to the patient the antibodies of claim 75, 76, 77, 78, 79, or 80.

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83. A method of treating a patient exposed to HCV, the method comprising steps of:
providing a patient exposed to HCV; and
administering to the patient the antibody of claim 75, 76, 77, 78, 79, or 80.

REMARKS

The present second Preliminary Amendment cancels claims 2, 24, 33-65, 68, 69, and 71-74 drawn to non-elected inventions without prejudice and adds new claims 75-83. Applicants reserve the right to pursue the canceled claims in any future divisional application. The new claims, drawn to antibodies specific for HCV E2 epitopes and corresponding pharmaceutical applications, fall within Group II, which is elected in the accompanying Response to Restriction/Election Requirement. Support for the new claims can be found in Figure 22 of the application. No new matter is introduced by the present second Preliminary Amendment.

It appears that the first Preliminary Amendment, filed February 11, 2002, was not entered because the new claims added in the first Preliminary Amendment were not considered by the Examiner in the Restriction/Election Requirement mailed on March 22, 2002. If the claims of the first Preliminary Amendment were entered, or have since been entered, please cancel these claims in favor of the claims added in the presently filed second Preliminary Amendment.

Attached hereto is a marked-up version of the changes made to the specification by the current amendment. The attached page is captioned "Version with Markings to Show Changes Made." Please charge any fees or credit any overpayments to our Deposit Account No. 03-1721.

Respectfully submitted,

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Dated: April 22, 2002

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I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Assistant Commissioner For Patents, Washington, D.C. 20231 on April 22, 2002

Ruth H. Hargrave



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In the Claims:

Claims 2, 24, 33-65, 68, 69, and 71-74 have been canceled.

Claims 75-83 have been added.

--75. A combination of two or more antibodies directed to one or more conformational epitopes of E2 protein of Hepatitis C virus.

76. The combination of two or more antibodies of claim 75, wherein the combination results in increased binding of the antibodies to one or more conformational epitopes of E2 protein of Hepatitis C virus.

77. The combination of two or more antibodies of claim 76, wherein the increased binding of two or more antibodies to the one or more conformational epitopes of E2 protein of Hepatitis C virus is greater than 100% relative to the binding of a single antibody.

78. The combination of two or more antibodies of claim 75 comprising CBH-7 and CBH-4G.

79. The combination of two or more antibodies of claim 75 comprising CBH-7 and CBH-4D.

80. The combination of two or more antibodies of claim 75 comprising CBH-7 and CBH-17.

81. A pharmaceutical composition comprising the antibodies of claim 75, 76, 77, 78, 79, or 80 and a pharmaceutically acceptable excipient.

82. A method of treating a patient infected with HCV, the method comprising steps of:
providing a patient infected with HCV or susceptible to HCV infection; and
administering to the patient the antibodies of claim 75, 76, 77, 78, 79, or 80.

83. A method of treating a patient exposed to HCV, the method comprising steps of:

providing a patient exposed to HCV; and
administering to the patient the antibody of claim 75, 76, 77, 78, 79, or 80.--



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Attorney Docket No. 2002850-0009

(S98-161 CIP II)

Claims Pending Restriction Election

1. An antibody directed to a conformational epitope of a protein of Hepatitis C virus.
3. An antibody directed to a conformational epitope of E2 protein of Hepatitis C virus.
4. The antibody of claim 1 wherein the dissociation constant (K_D) of the antibody for its epitope is less than 10^{-7} M.
5. The antibody of claim 1 wherein the binding constant (K_D) of the antibody for its epitope is less than 10^{-8} M.
6. The antibody of claim 1 wherein the binding constant (K_D) of the antibody for its epitope is less than 10^{-9} M.
7. The antibody of claim 1 wherein the binding constant (K_D) of the antibody for its epitope is less than 10^{-10} M.
8. An antibody directed to a conformational epitope within amino acids 411 through 644 of E2 protein of Hepatitis C virus 1b.
9. An antibody directed to a conformational epitope within amino acids 470 through 644 of E2 protein of Hepatitis C virus 1b.
10. An antibody directed to a conformation epitope within amino acids 470 through 644 of E2 protein of Hepatitis C virus 1b and exhibits minimal cross-competition with the antibodies of claim 8.

11. An antibody directed to an epitope within amino acids 644 through 661 of E2 protein of Hepatitis C virus 1b.
12. An antibody directed to the epitope recognized by CBH-2, -4D, -4B, -4G, -5, -7, -8C, -8E, -9, -11, or -17.
13. An antibody wherein the antibody competes with CBH-2, -4D, -4B, -4G, -5, -7, -8C, -8E, -9, -11, or -17 for binding to its epitope.
14. The antibody of claim 3 wherein the antibody inhibits binding of HCV E2 to CD81.
15. A cell line expressing the antibody of claim 1.
16. The cell line of claim 15 wherein the cell line is a B cell line.
17. The cell line of claim 15 wherein the cell line is a human cell line.
18. The cell line of claim 15 wherein the cell line is a mammalian cell line.
19. The cell line of claim 15 wherein the cell line is a eukaryotic cell line.
20. The cell line of claim 15 wherein the cell line is a hybridoma.
21. The cell line of claim 15 wherein the cell line has been transformed with Epstein-Barr virus (EBV).
22. The cell line of claim 15 wherein the cell line has been infected with a virus.
23. The cell line of claim 15 wherein the cell line has been infected with phage.

25. The antibody of claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or 13 wherein the antibody is a monoclonal antibody.
26. The antibody of claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or 13 wherein the antibody is a human antibody.
27. The antibody of claim 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, or 13 wherein the antibody is a humanized antibody.
28. The antibody of claim 1 wherein the antibody is a mammalian antibody.
29. A pharmaceutical composition comprising the antibody of claim 1 and a pharmaceutically acceptable excipient.
30. A method of treating a patient infected with HCV, the method comprising steps of:
providing a patient infected with HCV or susceptible to HCV infection; and
administering to the patient the antibody of claim 1.
31. A method of treating a patient exposed to HCV, the method comprising steps of:
providing a patient exposed to HCV; and
administering to the patient the antibody of claim 1.
32. The method of claim 30 or 31 wherein the step of administering the antibody comprises administering more than one different antibody.
66. A method of classifying patients infected with HCV, the method comprising steps of:
providing serum from a patient infected with HCV;
measuring inhibition by the patient's serum of binding of an anti-HCV monoclonal antibody to its epitope; and
identifying patient as candidate for administration of a treatment.

67. The method of claim 66, the method comprising additional step of:
administering to the patient an antibody.
70. The method of claim 66, wherein the step of administering comprises administering an antibody directed to the epitope that is bound by an anti-HCV monoclonal antibody, the binding of which is not inhibited by the patient's serum.
75. A combination of two or more antibodies directed to one or more conformational epitopes of E2 protein of Hepatitis C virus.
76. The combination of two or more antibodies of claim 75, wherein the combination results in increased binding of the antibodies to one or more conformational epitopes of E2 protein of Hepatitis C virus.
77. The combination of two or more antibodies of claim 76, wherein the increased binding of two or more antibodies to the one or more conformational epitopes of E2 protein of Hepatitis C virus is greater than 100% relative to the binding of a single antibody.
78. The combination of two or more antibodies of claim 75 comprising CBH-7 and CBH-4G.
79. The combination of two or more antibodies of claim 75 comprising CBH-7 and CBH-4D.
80. The combination of two or more antibodies of claim 75 comprising CBH-7 and CBH-17.
81. A pharmaceutical composition comprising the antibodies of claim 75, 76, 77, 78, 79, or 80 and a pharmaceutically acceptable excipient.
82. A method of treating a patient infected with HCV, the method comprising steps of:
providing a patient infected with HCV or susceptible to HCV infection; and
administering to the patient the antibodies of claim 75, 76, 77, 78, 79, or 80.

83. A method of treating a patient exposed to HCV, the method comprising steps of:
providing a patient exposed to HCV; and
administering to the patient the antibody of claim 75, 76, 77, 78, 79, or 80.